

REMARKS/ARGUMENTS

FORMAL MATTERS

Claims 1-20 are pending after entry of the amendments set forth herein. Claims 1-8 and 16-20 stand withdrawn as directed to non-elected subject matter.

With this response, claims 9 and 13 are amended to recite pathogenic bacteria, rather than bacterium. Support for these amendments may be found throughout the specification, such as, for example at paragraphs 116 and 117. Thus, after entry of these amendments, claims 9-15 are under examination on the merits. No new matter is added by way of these amendments, therefore, entry is respectfully requested.

DOUBLE PATENTING

Claims 9-10 and 13-14 were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1, 3-4 and 8-9 of U.S. Patent No. 6,913,753. A Terminal Disclaimer prepared in accordance with 37 C.F.R. § 1.321(b) and (c) will be submitted to obviate the obviousness-type double patenting rejection and withdrawal is respectfully requested.

REJECTION UNDER § 112, ¶ 2

Rejection of claims 9-15

Claims 9-15 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite in the recitation of the phrase "incapacitated whole cell bacterial vaccine". In the process of construing a claim's meaning, one must first look to the definitions provided in the specification. *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 116 S. Ct. 1384 (1996). Only if no definition is set forth in Applicants' specification does one then consider the ordinary, plain meaning of a term. *See, e.g., Vitronics Corp. v. Conceptronic, Inc.*, 90 F3d 1576 (Fed. Cir. 1996).

Here, the Examiner has looked to the dictionary in order to present the plain meaning of the term "incapacitated". However, at page 10, para. [0042] of the specification, Applicants teach that:

"By 'incapacitated' in the context of an incapacitated bacterial cell produced according to the invention, is meant that the bacterial cell is in a state of irreversible bacteriostasis. While the bacterium retains its structure -- and thus retains the immunogenicity, antigenicity, and receptor-ligand interactions associated with a wild-type bacterium -- it is not capable of replicating due to the depletion of host factors due to the expression from a recombinant promoter."

Where Applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that Applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357 (Fed. Cir. 1999); MPEP 706.03(d) ¶ 7.34.02.

Applicants' specification clearly defines "incapacitated" in the context of a bacterial cell, as a cell that retains its structure, but is not capable of replicating due to overexpression of a gene(s) under the control of a recombinant promoter, such as T7. At page 15, para. [0063], for example, the specification teaches that "incapacitated bacteria of the invention are produced by expression, particularly hyper-expression, from a recombinant promoter. Expression from the recombinant promoter is at a level sufficient to render the bacterial host bacteriostatic."

New terms are often used when a new technology is in its infancy or is rapidly evolving. MPEP §706.03(d) ¶ 7.34.02. If the claims, read in light of the specification, reasonably apprise those skilled in the art both of the utilization and scope of the invention, and if the language is as precise as the subject matter permits, the statute (35 U.S.C. § 112, second paragraph) demands no more. *Shatterproof Glass Corp. v. Libbey Owens Ford Co.*, 758 F.2d 613 (Fed. Cir. 1985) (interpretation of "freely supporting" in method claims directed to treatment of a glass sheet); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 USPQ 81 (Fed. Cir. 1986) (interpretation of a limitation specifying a numerical value for antibody affinity where the method of calculation was known in the art at the time of filing to be imprecise).

Thus, Applicants submit that use of the phrase "incapacitated whole cell bacterial vaccine" in claims 9-15 is not indefinite in light of the specific definitions provided in Applicants' specification.

Rejection of claims 9 and 13

Claims 9 and 13 stand rejected under 35 U.S.C. § 112, ¶2 as allegedly indefinite in the recitation of the singular term "bacterium". With entry of the amendments set forth above, Applicants submit that the instant claims are allowable in their current form and the rejection may be withdrawn.

REJECTIONS UNDER § 102

Claims 9-10 and 13-15 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Marjarian et al. (U.S. Patent No. 6,130,082). This rejection is respectfully traversed for at least the following reasons.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Independent claim 9 is drawn to "[a] method of vaccinating a subject against disease caused by a bacterial pathogen, the method comprising:

administering to a subject susceptible to disease caused by pathogenic bacteria an incapacitated whole cell bacterial vaccine, the vaccine comprising the pathogenic bacteria incapacitated by expression from a recombinant promoter operably linked to a polynucleotide encoding a gene product, said administering being in an amount effective to elicit an immune response to pathogenic bacteria in the subject."

Marjarian et al. disclose that the recombinant flagellin genes of their invention are expressed in live, "attenuated invasive bacteria" (*see* col. 18; lines 23-24 and line 40). "Preferably, the bacterium is live and infectious but cannot cause significant disease in the vertebrate host" (*see* col. 9; lines 6-10). Applicants' independent claims recite the use of *incapacitated* bacteria. Applicants' specification discloses that "incapacitated" in the context of a bacterial cell produced according to the invention means that the cell is in a state of irreversible

bacteriostasis. The bacterium retains its structure, and thus, retains its immunogenicity and antigenicity, but it is not capable of replicating due to the depletion of host factors from overexpression of genes under the control of a recombinant promoter (*see, e.g.,* the Specification at page 10, para. [0042]). The attenuated invasive bacteria of Marjarian et al. are live and capable of replication. They express a recombinant flagellin necessary for motility and replication. Marjarian et al. neither teach nor disclose the use of incapacitated bacteria, and therefore would not lead one of ordinary skill to appreciate the use of bacteria that retain their structure but are in a state of irreversible bacteriostasis.

Accordingly, Marjarian et al. cannot anticipate these claims.

REJECTIONS UNDER § 103(a)

Claims 9-15 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Marjarian et al., Kordyum et al., and Wright et al. This rejection is respectfully traversed for at least the reasons set forth below.

We first provide a brief review of the relevant law, and then analysis of the facts of the case at hand.

The law of obviousness requires that the differences between the prior art and the claimed invention be evaluated at the time the invention was made, and without benefit of Applicants' disclosure

As set forth in MPEP § 2141 (I),¹ the four factual inquires for determining obviousness are as follows:

- (A) Determining the scope and contents of the prior art;
- (B) Ascertaining the *differences between the prior art and the claims in issue*;
- (C) Resolving the level of ordinary skill in the pertinent art; and
- (D) Evaluating evidence of secondary considerations.

The differences between the claimed invention and the prior art must be evaluated "at the time the invention was made" in order to avoid impermissible hindsight.²

¹ Citing *Graham v. John Deere*, 383 U.S. 1, 148 USPQ 459 (1966).

Furthermore, analysis of obviousness requires consideration of the claimed invention as a whole,³ as well as consideration of the *entire* disclosure of any prior art reference applied against the claims, including portions that would lead away from the claimed invention.⁴

A prima facie case of obviousness requires an Examiner to provide an explicit reason why the skilled worker would combine the known elements in the fashion claimed by Applicant

The Patent Office bears the burden of establishing a *prima facie* case of obviousness under 35 U.S.C. § 103. *In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988); *In re Duel*, 51 F.3d 1557 (Fed. Cir. 1995). To support a rejection under § 103 using the Federal Circuit's teaching-suggestion-motivation (TSM) test, the Office must provide evidence that demonstrates some suggestion or motivation to modify or combine the references, whether in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *Fine*, 837 F.2d at 1074; MPEP § 2143. Next, the Office must show that one of ordinary skill in the art would have had a reasonable expectation of success in modifying the prior art references, or in combining their relevant teachings. *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991). Finally, the Office must show that the combined prior art references "teach or suggest all the claim[ed] limitations." MPEP § 2143.

Recently, in reviewing this standard, the Supreme Court noted that any analysis supporting a rejection under § 103(a) must be made explicit, and that it is "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the

² 35 U.S.C. § 103(a) states:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, *if the differences* between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious *at the time the invention was made* to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made (emphasis added).

³ See, e.g., MPEP § 2141.02 (I).

⁴ See MPEP § 2141.02 (VI) ("A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention.").

[prior art] elements in the manner claimed." *KSR Intl Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (U.S. 2007). "This is so because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." *Id.*

The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure.⁵ The Examiner's suggestion of the desirability of doing what the inventor has done must be found either expressly or impliedly in the references, or supported by a convincing line of reasoning, which must rely on logic and sound scientific reasoning.⁶ While the Court warned against a "rigid application"⁷ of the TSM test, the Court also found that these questions could provide a "helpful insight" in determining whether the claimed subject matter is obvious under § 103(a).⁸

Applicants submit that the Office has failed to present a *prima facie* case of obviousness. To meet its burden in establishing a rejection under § 103 using the Federal Circuit's TSM test, the Office must show that the cited art teaches or suggests all the claim limitations. MPEP § 2143.

Independent claim 9 is drawn to "[a] method of vaccinating a subject against disease caused by a bacterial pathogen, the method comprising:

administering to a subject susceptible to disease caused by pathogenic bacteria an incapacitated whole cell bacterial vaccine, the vaccine comprising the pathogenic bacteria incapacitated by expression from a recombinant promoter operably linked to a polynucleotide

⁵ *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

⁶ *Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985). *See also* MPEP § 2144; and *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993) (requiring reliance on logic and sound scientific reasoning in supporting a conclusion of obviousness).

⁷ *KSR*, slip op. at 15.

⁸ *KSR* slip op. at 14. *See also*, Memorandum to Technology Directors from Margaret A. Focarino, Deputy Commissioner for Patent Operations, May 3, 2007.

encoding a gene product, said administering being in an amount effective to elicit an immune response to pathogenic bacteria in the subject," (emphasis added).

The Examiner acknowledges that claims 9-15 are not obvious in view of Marjarian et al. alone as "they don't disclose the recombinant expression of a protein that binds LPS generally or LPS binding protein specifically."

While this is correct, Marjarian et al. additionally neither shows nor suggests the use of incapacitated bacteria, and therefore would not lead one of ordinary skill to appreciate the use of bacteria that retain their structure but are in a state of irreversible bacteriostasis. As Kordyum and Wright were cited solely for their alleged disclosure of the T7 promoter system and the LPS binding protein functionality, respectively, neither reference can cure the stated deficiency and a *prima facie* case of obviousness has not been shown.

Even if, *in arguendo*, the Office could establish a teaching of all the claimed features, Marjarian et al. teach the use of previously attenuated bacteria (*see* col. 16, lines 17-18). In contrast, the claimed method arises from the surprising discovery that "hyper-expression" of nearly any gene may be employed to incapacitate the administered bacteria. The data presented in the specification demonstrate that "...incapacitation may be achieved even by simply expressing T7 RNA polymerase," (*see* specification at page 16, lines 1-2). This unexpected property of the bacteria used in Applicants' claimed method is further described in the specification, for example at page 15, para. [0067] through page 16, para. [0068] and FIGS. 1-2. According to Applicants' method, incapacitation may be achieved via hyper-expression of any gene, including GFP, which does not have any known, specific activity resulting in inactivation. As such, the bacteria of Applicants' method are not previously attenuated and Applicants' finding would not have been predictable to the skilled worker. Applicants perform a specific step rather than mere culture passaging, traditionally used to attenuate bacteria. Passaging over time causes bacteria to lose characteristics required for authentic immunogenicity and antigenicity. Moreover, Applicants' method is simpler in that the skilled worker does not have to use alternative strains of bacteria. Thus, the cited art does not predict that incapacitation may be achieved simply by hyper-expression of otherwise benign genes.

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PATENT

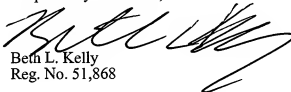
Accordingly, the cited references neither alone nor when combined render the claimed subject matter obvious and this rejection should be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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